Hypernatremia

Its Significance in Pediatric Practice

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• Hypernatremic dehydration is a fairly common and potentially very dangerous illness in infants and children. It occurs during the course of a wide variety of illnesses.

Predisposing factors include central nervous system diseases, decreased fluid intake, increased fluid losses from hyperventilation, perspiring, diarrhea and emesis, increased aldosterone output (contributing to sodium retention), the infant's high obligatory renal water loss and the practice of feeding infants fluids with a comparatively high solute content.

If the attending physician is aware of the predisposing factors and makes an early diagnosis and then rehydrates the patient slowly using solutions which contain some salt, the outcome will most likely be favorable. Even though the brain appears to be damaged during rehydration, the patient may make a complete recovery if proper supportive measures are instituted.

ALTHOUGH HYPERNATREMIA (serum sodium concentration of 150 mEq. per liter or more) is by definition a laboratory diagnosis, early evaluation and proper management remain largely a clinical responsibility. Because delayed or inappropriate therapy can lead to irreversible brain damage or death, it behooves every physician who cares for sick children to acquire an understanding of hypernatremic dehydration. The purpose of this paper is to review the factors of clinical significance in practice and to present some of the findings in a study of 93 infants and children with hypernatremia at the Children's Hospital of the East Bay in Oakland.

PREDISPOSING FACTORS

Several predisposing factors make infants peculiarly susceptible to the development of hypernatremic dehydration (Figure 1). A relatively large surface area permits a correspondingly increased evaporative loss of water from the skin and lungs (insensible loss). This loss is greatly magnified when there is sweating in response to fever or environmental heat and when there is hyperventilation due to respiratory disease, acidosis, fever and crying.

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HYPERNATREMIA - PREDISPOSING FACTORS

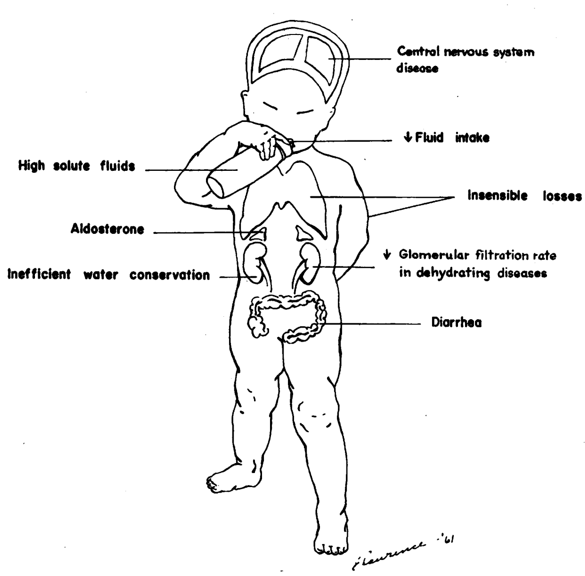

Figure 1.—Factors predisposing to the development of hypernatremia in infants and children.

Approximately one out of five children admitted to the hospital for diarrhea has hypernatremic dehydration. The role of diarrhea in the production of hypernatremia has been particularly emphasized and perhaps overemphasized. This may reflect the frequency of diarrhea in infants and the fact that pediatricians have been trained to observe serum electrolyte content in such patients with great diligence. A recent study[10] showed no correlation between sodium loss in diarrheal stools and serum sodium values, but diarrheal stools that produce a greater loss of fluid than of electrolytes may be significant.

A less apparent but perhaps more fundamental etiologic factor is to be found in the infant's immature and normally inefficient renal concentration mechanism that requires a persistently high obligatory loss of renal water. Furthermore, a dehydrated sick infant is able to conserve water even less efficiently than a normal infant. It has been shown that both the glomerular filtration rate and the urea clearance are decreased in dehydrating diseases.[1] Factors such as fever and the disease itself which augment tissue breakdown will increase the solute load. When in addition there is underlying renal disease, the infant is further handicapped. (Six per cent of the patients in the present study had serious renal diseases.)

Central nervous system diseases in children (cerebral concussion, mental retardation, brain tumor, meningitis, subdural hygroma) predispose toward hypernatremia even when there has been no dehydration.[3] This effect is possibly mediated through aldosterone, since it has been shown that a hormone adrenoglomerulotropin produced in the region of the pineal gland influences the production of aldosterone.[6] Aldosterone causes a decrease in renal sodium excretion. (In the present series 14 per cent were mentally retarded, 1 per cent had brain tumor and 3 per cent had meningitis.)

All the above factors may be compounded by the fact that a sick infant invariably fails to ingest adequate quantities of fluids. In addition, many are given boiled skim milk and other fluids high in electrolyte content as therapy for the diarrhea. Skim milk has a higher amino acid and electrolyte content per ounce than whole milk and therefore presents an additional solute load to the kidney at a time when the infant is less able to handle it. Even giving dilute hypotonic electrolyte solutions may not prevent the development of hypernatremia unless enough extra water is given to cover not only the diarrheal losses but also the increased insensible losses.[7]

CLINICAL DIAGNOSIS

Essential to an early diagnosis of hypernatremia is a physician with a high index of suspicion. Actually, the baby's appearance may be deceptively good until dehydration has become severe. Because two-thirds of the water lost in hypernatremic dehydration is intracellular water, the skin turgor may well be normal despite a loss of 10 per cent or more of the body weight.[9] Also vascular collapse comes rather late in the disease since only one-third of the water loss involves the extracellular compartment. When vascular collapse (shock) does occur, it is likely to be precipitous and a late and ominous sign.

Symptoms referable to the central nervous system are frequent, especially pronounced irritability, muscular hypertonicity, convulsions and stupor. These symptoms may be so pronounced that the physician will suspect meningitis; and if a lumbar puncture is done, the spinal fluid protein is likely to be found to be elevated.[11]

The initial history may lead the physician to suspect hypernatremia if he questions carefully as to exact fluid intake. Data from the present study indicate, however, that there are many instances in which hypernatremia cannot be predicted on the basis of the history and suggest that greater emphasis be placed on obtaining initial serum electrolyte determinations in any child with moderate to severe dehydration from any cause.

PATHOLOGIC PHYSIOLOGY

Why does a patient with hypernatremic dehydration have so many central nervous system manifestations? The degree of dehydration may not be any greater than in a patient with isotonic dehydration; and, yet, the hypernatremic patient is likely to have a more difficult time.

All hypertonic solutions produce tissue dehydration. Experimentally, the central nervous system symptoms produced by the infusion of hypertonic sodium solutions are, however, more severe than the symptoms due to the infusion of equally hypertonic solutions of sucrose or urea. This is presumably because sucrose and urea diffuse into central nervous system cells to equalize osmolarity; whereas, sodium does not.[9] In order for the central nervous system cells to increase their osmolarity to that of the hypernatremic extracellular fluid, two things are thought to occur: (1) water leaves the central nervous system cells and (2) the intracellular proteins break down to form intracellular solutes (potassium and amino acids). The severe disruption of intracellular proteins could, of course, account for the drastic and sometimes permanent impairment of brain function.

Severely dehydrated hypernatremic infants (and kittens) are known to develop cerebral petechiae, subdural effusions, subdural hematomas and cerebral vein thrombosis.[8,9] To what extent the vascular alterations are due to dehydration alone and to what extent they are due to combined dehydration and hypernatremia is not, at present, clear.

Physicians should be aware that central nervous system symptoms can be precipitated by infusing electrolyte-free or highly dilute fluids too rapidly during therapy. Sudden dilution of the extracellular fluid frequently initiates convulsions. Such convulsions have been terminated by reinfusing with hypertonic saline solution until the serum sodium returned to the same high level that was present before therapy was begun.[23]

Even with optimal fluid therapy, a hypernatremic patient occasionally retains water in inappropriate amounts. When this occurs, the extracellular fluid volume overexpands and produces symptoms (such as convulsions, irritability, lethargy and unconsciousness). This was demonstrated by balance studies on 11 infants with hypernatremia and gastroenteritis. The five infants who had convulsions retained water inappropriately and formed a scant amount of urine after intravenous therapy was begun; whereas the six infants who did not become

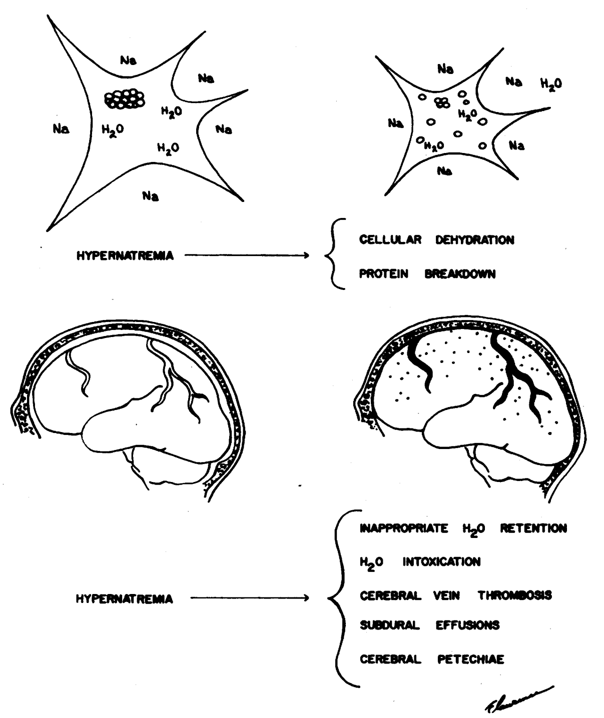

Figure 2.—Mechanisms by which a patient with hypernatremia develops central nervous system symptoms: The brain cells lose water and shrink and the intracellular protein molecules break down. The complications illustrated in the bottom half of the figure occur frequently.

severely ill and did not have convulsions began forming dilute urine as soon as intravenous therapy was begun.[16]

In dogs, experimentally induced hypernatremia (both with and without dehydration) produces renal tubular necrosis.[12] (In the one patient in the present series who died as a result of hypernatremic dehydration, hemorrhagic necrosis of the renal papillae was observed on postmortem examination.)

Aldosterone output (aiding retention of sodium) is increased in dogs dehydrated by inducing vomiting or withholding fluids; and there is some evidence that this also occurs in humans.[14] If so, one wonders why hypernatremia does not occur even more frequently than it does.

REPORT OF STUDY

During a 13-month period at the Children's Hospital of the East Bay, 93 patients were reported to have serum sodium values of 150 mEq. per liter or more; in 20 the content was found to be 160 mEq. per liter or more; in two it was over 190 mEq. Fifty-six per cent of these hypernatremic patients were under one year of age. Most papers dealing with hypernatremia have emphasized the importance of diarrhea or of excess salt intake or both as predisposing to the development of elevated serum sodium concentrations. In the present study only a slight majority (56 per cent) had diarrheal disease. Only four patients had a definite history of excess salt intake—two by oral intake of electrolyte solutions and two in parenteral fluids.

Table 1 lists the diagnoses in the surviving patients who did not have diarrheal disease. Table 2 lists the primary causes of death in 16 patients who died. Only one died as a direct result of hypernatremic dehydration. Necropsy revealed dural sinus thromboses, subdural hematomas and hemorrhagic necrosis of the renal papillae.

TABLE 1.—*Primary Diagnosis in 28 Living Patients with Hypernatremia*

Na Over 150 mEq. per Liter	No. Cases
Dysautonomia	1
Pneumonia	1
Intussusception, volvulus	1
Pneumococcal sepsis	1
Pyloric stenosis	2
Diabetes	3
Exstrophy bladder, ureters in colon	1
Cystic fibrosis	1
Meningococcemia	1
Acetyl salicylic acid ingestion	3
Milk allergy	3
Nephrosis	1
Meningoencephalitis	3
Burn	1
Hypophosphatemic rickets	1
Na Over 160 mEq. per Liter	
Tuberculosis, pulmonary	1
Megacolon, Fleet enema	1
Intussusception, volvulus	1
Cleft palate with otitis media	1

TABLE 2.—*Primary Causes of Death in 16 Patients with Hypernatremia*

Na Over 150 mEq. per Liter	No. Cases
Cystic fibrosis	1
Congenital heart disease	4
Chloromycetin intoxication	1
Renal disease	2
Leukemia	1
Arsenic intoxication	1
Volvulus, perforation	2
Pneumococcal pneumonia	1
Na Over 160 mEq. per Liter	
Brain tumor	1
Myocarditis	1
Dehydration, dural sinus thrombosis, subdural hematoma	1

TREATMENT

Primary in the treatment of any severely dehydrated patient is the replacement of fluid losses by appropriate intravenous therapy.

If the patient is in shock, a compelling emergency exists; and the fluid given should be such as to expand the intravascular compartment even though on admission one may not know the state of hypernatremia or hyponatremia. Plasmanate®* has proved to be very useful in this regard. Plasmanate® re-

*Cutter, 5 per cent reconstituted human serum protein solution.

quires neither refrigerator storage nor the typing necessary for blood and does not carry the risk of transmitting hepatitis.

If the patient is not in shock, the safest solution for initial hydration is N/3 saline (0.3 per cent) in 5 per cent glucose solution while waiting for the laboratory to report initial electrolyte values. If the patient is hypernatremic, further therapy is planned to bring the electrolytes into balance slowly by using hypotonic (0.11 per cent to 0.2 per cent) saline in 5 per cent glucose solution. (This provides 17 to 30 mEq. of sodium per liter.) It is necessary that the hydrating solutions contain some sodium if water intoxication (which occurs relatively easily in hypernatremia) is to be avoided. There are fewer nervous system complications if rehydrating solutions contain from 15 to 45 mEq. of sodium per liter. The surviving patients in the present series, observed for 10 to 12 months after recovery, did not have mental damage.

In one case in the series apnea resulting from central nervous system depression was successfully treated with intermittent positive pressure breathing. Complete rehydration and correction of the serum sodium need not and should not be rapid. Actually, once a patient is out of shock, there is no need for haste; and, in fact, it is impossible to correct severe hypernatremia rapidly. Patients do best when the serum sodium content is gradually brought back to normal over a period of two or three days.

A rough estimate of the degree of dehydration can be made if the patient's weight immediately before the dehydrating episode is known. If an infant is calculated to be over "10 per cent dehydrated" (10 per cent weight loss), he will need about 100 ml. of fluid per pound of body weight for the first day; if between 5 and 10 per cent dehydrated, about 80 ml. per pound for the first day; and if less than 5 per cent dehydrated, about 60 ml. per pound.

By the second or third day, when rehydration is well under way, the quantities of fluids required are reduced to approximately the amounts shown in Table 3.

All fluid therapy must be evaluated daily, and sometimes on an hourly basis, depending on the patient's output and the serum electrolyte determinations. All forms of fluid output must be considered: urine, diarrhea, sweating, hyperventilation, emesis and fluid suctioned off from the gastrointestinal tract.

If the patient is both dehydrated and in heart failure—as sometimes occurs, digoxin is used along with intravenous fluids. Both the heart failure and the dehydration must be treated simultaneously. Digoxin is preferred for infants and children because of its quick action and fairly rapid elimination. For infants under two years of age, the digitalizing dose is 0.03 to 0.04 mg. per pound of body weight. Half that amount is given as the first dose, with the remainder divided equally and given at eight-hour intervals or more frequently, according to need. For older children, the digitalizing dose is 0.02 to 0.03 mg. per pound of body weight. The maintenance digoxin dose is from one-fifth to one-third of the total digitalizing dose per day.

The sequence of events in the treatment can be summarized as follows: Evaluating of the degree of dehydration; determining whether shock or heart failure is present; determining the electrolyte contents of the blood. Then initial intravenous fluid therapy: Plasmanate® (plasma substitute) if the patient is in shock; otherwise, 0.3 per cent saline in 5 per cent glucose solution while awaiting laboratory reports.

After renal function is established (urination), potassium is added in amount of 3 mEq. per kilogram of body weight per day (not to exceed 40 mEq. per liter) to the intravenous fluids until oral feedings are established.

Other supportive measures that may be needed are: digoxin, if in heart failure; antibiotics, if bacterial infection suspected; calcium gluconate, for tetany which may occur when the acidosis is corrected and the serum calcium is low or borderline; intermittent positive pressure breathing for respiratory failure; subdural taps, if there is persistent unexplained fever or continued convulsion; and phenobarbital or other anticonvulsants.

TABLE 3.—*Amount of Fluid (0.2 Per Cent Saline in 5 Per Cent Glucose) Required Daily for Normal Maintenance of Hypernatremic Patients*

	Milliliters per Day		
	Per Pound of Body		Per Kg. of Body
Premature infants over 7 days old	75	or	150
Infants under 1 year	60		125-150
Children 1 to 5 years	50		100-125
Children 5 to 10 years	30-40		75-100

Once renal function is established, add potassium in amounts of 3 mEq. per kg. of body weight.

TABLE 4.—*Caloric, Sodium and Potassium Content of Fluids Commonly Given to Infants*

	Calories per Liter	Na mEq./l	K mEq./l	Mg. N/l
Human milk	650	7	14	1920
Cow's milk (whole)	670	22	36	5300
Cow's milk (skim)	375	23	37	
Orange juice	500	0.2	49	
Apple juice	480	1.7	26	
Pineapple juice	500	0.2	36	
Ginger ale	360	3.5	0.1	
Coca-Cola	435	0.4	13	
Lytren®*	280	50	20	

*A concentrated solution of electrolytes.

PREVENTION

Foremost in the prevention of hypernatremia is an awareness on the part of all physicians that this condition is fairly common (occurring in 10 to 33 per cent of infants put in hospital for diarrhea) and the realization that it results from a combination of factors including diminished intake of water, diarrhea, hyperventilation, sweating, excessive salt intake and protein breakdown. Prevention begins at home as soon as the physician is aware that the child is ill. The mother should encourage the child to maintain adequate fluid intake, and this fluid should contain a lower concentration of salt than the patient normally takes. This is necessary in order to provide fluid for the increased insensible losses (through the skin and lungs) that occur with illness of any kind. Both skim and whole milk contain salt (Table 4). In order to provide extra water during illness, the mother should dilute the milk and add sugar. The extra sugar will help to delay tissue breakdown and at the same time make the milk more palatable. Fruit juices, ginger ale and Coca-Cola contain about a tenth as much sodium as milk and are very useful supplements or substitutes for milk when infants and children are ill.

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